Editorial

Imatinib in India: Is the efficacy universal?

Since the discovery of the "minute chromosome"[1] in 1960 by Nowell and Hungerford and Janet Rowely's[2,3] description of the consistent chromosomal abnormality more than a decade later in patients with a diagnosis of chronic myeloid leukemia (CML) there have been significant strides made in the management of this condition, culminating in the recent past with the introduction of Imatinib.

In June 1998, the drug was given to the first human volunteer with CML in phase I trials[4,5]. Here patients were either unresponsive to interferon (IFN), the then standard of care in chronic phase or were patients who had progressed to an accelerated phase or were in blast crisis. In the next three phase II trials, the efficacy of this drug in all phases of CML was confirmed[6-8]. However, it was the landmark phase III trials that established its status as the first line drug of choice in the management of newly diagnosed cases of CML. These trials established beyond doubt the superior cytogenetic response rates and duration of responses compared to the considered gold standard of IFN administered along with low dose cytosine[9,10].

Marketed by Novartis, Switzerland (Glivec) at a price of approximately Rs 100,000 per month, it was an affordable option only in the developed countries. Initially in the United States it was approved only for patients with INF unresponsive CML in chronic phase (CP) and for advanced phase. Subsequently, its use in newly diagnosed CML in CP was approved by US-FDA (Food and Drug Administration) in December 2002. Before the exclusive marketing rights (EMR) were granted to Novartis, many Indian companies launched Imatinib through reverse engineering and it was being marketed at a fraction of the cost of Glivec, but was still unaffordable to the majority of patients.

It was when Max foundation (started in memory of Maxmillano from Argentina who died of CML at the age of 17 yrs) supported the developing countries with its generous GIPAP (Glivec International Patient Assistance Programme) program that CML patients of 60 odd nations including India benefited. This program was initially restricted to patients resistant to INF unresponsive CML-CP or advanced phase disease. The program was opened for first line therapy for CML since April 2003. With the introduction of this efficient and well run program it is possible for practically every newly diagnosed patient with CML in India to be enrolled and treated with this drug. With the cost of the drug being absorbed by GIPAP, it has become the choice of front line therapy both because of the reduced cost of treatment and because of the proven benefit in this condition. The latter however was based on extrapolation from data generated from the West and it was potentially possible that there could be differences in both the efficacy and toxicity profile of this drug among Indian patients.

In this issue Arora et al have present their single center experience on the use of Imatinib in the treatment of CML.[11] This data represents the largest published experience from India and addresses key issues such as efficacy and toxicity in our population. In this study the complete haematological responses (CHR) in chronic phase was 96% and in the advanced phase group it was 45% with a median interval of 3 weeks and 4 weeks,

respectively to achieve it, which is comparable to the published data. However, the 30% major cytogenetic remission (MCR) and 24.5% complete cytogenetic remission (CCR) among patients with CML - CP is much lower than that reported in the literature. Published phase II trials in patients who had received prior IFN therapy and phase III trials with up front Imatinib therapy had MCR and CCR of 60% versus 85.2% and 40% versus 73.8% respectively[6,7,9,10]. In spite of the relatively lower cytogenetics response rate in this population, the data with Imatinib is still significantly better than the other pharmacologic alternatives currently available. The finding of a lower cytogenetics response rate in our population will need to be validated in larger multi-center trials before it can be accepted. In the intervening period it would be of interest to address the pharmacokinetic and pharmacogenetic variation in our population with reference to this drug which could further be influenced by nutritional status and dietary habits.

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